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10/727,537	12/05/2003	Thomas M. Woerner	033209-005	7356

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EXAMINER

FORD, ALLISON M

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 12/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/727,537	WOERNER, THOMAS M.	
	Examiner	Art Unit	
	Allison M Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-47 is/are pending in the application.
- 4a) Of the above claim(s) 10-21 and 43-47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 22-42 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-47 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-9, 22-42, drawn to a method of stabilizing solubilized phenyl phosphate and the stabilized solubilized phenyl phosphate produced, classified in class 436, subclass 126.
- II. Claims 10-12, drawn to a kit for phosphatase- phenyl phosphate reactions, classified in class 435, subclass 21.
- III. Claims 13-21, drawn to a method for recycling solubilized phenyl phosphate, classified in class 549, subclass 218.
- IV. Claims 43-47, drawn to a kit for recycling a solubilized phenyl phosphate, classified in class 423, subclass 364.

The inventions are distinct, each from the other because of the following reasons:

Invention II is related to Inventions I and III as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the kit of Invention II does not require the stabilized solubilized phenyl phosphate to be made by the methods of Inventions I or III. Applicant's disclosure teaches several other methods by which solubilized PNPP can be stabilized; for example, PNPP can be supplied in a solid matrix, by freeze drying or dry blending, or other modes of chemical immobilization. Alternatively PNPP can be stabilized in an aqueous solution by mixing the solution with imidazol and other nitro aliphatic compounds (US 4,132,598); or by dissolving the reagents in a water miscible organic solvent and supplementing the solution with an inert, high surface area, particulate desiccant. Though applicant finds shortcomings with these methods they still provide

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permissible means to produce stabilized solubilized phenyl phosphates to be used in the kits of Invention II; therefore the kits of Invention II do not require the methods of Inventions I or III.

Inventions I and III are distinct inventions and thus are subject to restriction. The inventions are distinct processes in that the methods are not dependent on each other, not to be used together and have different functions, modes of operation, and effects. In the instant case the method of Invention I requires use of whole phenyl phosphates, which is not used by the method of Invention III. The method of Invention III requires colored phenyl phosphates, which have already been hydrolyzed, which are not used by the method of Invention I. Therefore the methods do not use the same substrates, and thus have different modes of operation, and different final effects.

Invention IV is related to Inventions I and III as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the kit of Invention IV contains only charcoal. Charcoal can be used for purposes other than the stabilizing of a solubilized phenyl phosphate (Invention I) or the recycling of a solubilized phenyl phosphate (Invention III). For example, the kit with the charcoal, especially in a tablet form, can be used for medicinal purposes, such as for relieving an upset stomach. Additionally, it has been shown that phenyl phosphate can be stabilized by methods that do not employ charcoal (see teachings above).

Inventions II and IV are distinct inventions and thus are subject to restriction. The inventions are distinct in that the products are not dependent on each other, not to be used together and have different functions, modes of operation, and effects. In the instant case the kits of Inventions II and IV contain

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completely different products. The kit of Invention II requires a phosphatase enzyme and a stabilized phenyl phosphate, neither of which are included in the kit of Invention IV. The kit of Invention IV requires charcoal, which is not included in the kit of Invention II. Furthermore, these kits are not to be used together; the charcoal in the kit of Invention IV is for stabilizing solubilized phenyl phosphate, the kit of Invention I already includes stabilized, solubilized phenyl phosphate.

Therefore, a search and examination of all inventions in one patent application would result in an undue burden. These inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, different classifications, and a search for one group does not require a search for another group, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ms. Meyers on 11/2/04 a provisional election was made with traverse to prosecute the invention of Invention I, claims 1-9 and 22-42. Affirmation of this election must be made by applicant in replying to this Office action. Claims 10-21 and 43-47 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The traversal is on the ground(s) that there is no burden of search between Groups I and II, as the kit of Invention II only requires the assembly of the components used in the method of Group I. This is not found persuasive because the kit of Invention II only requires a stabilized solution of phenyl phosphate, it does not require the phenyl phosphate to be stabilized by the method of Invention I. Applicant discloses several methods that can be used to stabilize phenyl phosphate which do not utilize charcoal; therefore the product used in the kit of Invention II can be made by other methods than the method of Invention I. The requirement is still deemed proper and is therefore made FINAL.

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Status of the Application

Claims 1-9 and 22-42 are being examined for patentability. Claims 1-47 are pending in the current application, of which 10-21 and 43-47 have been withdrawn from consideration.

Specification

The disclosure is objected to because in Table V the amount of PNPP added is not clear. PNPP is in solution, at concentrations of 50 mg/mL to 200 mg/mL; however in the first column there is no unit for the amount of PNPP added, only 1.0 PNPP. In the remaining columns the PNPP is measured in grams, it appears all the units should be in milliliters; as is, it is not clear how much PNPP was added.

Additionally, the amount of AMPD buffer added is reported in grams, as buffer is a liquid; it appears these units should be reported as milliliters or other volumetric units. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 recites the limitation "the phenyl phosphate" in line 1 of the claim. Because claim 2 is dependent on claim 1, the phenyl phosphate must be solubilized; thus the claim should read, "The method of claim 1, wherein the solubilized phenyl phosphate is paranitrophenyl phosphate. As currently written, claims 3-5 and 9 recite the limitation "the solubilized phenyl phosphate" in the first lines of the claims, there is insufficient antecedent basis in parent claim 2 for this limitation in the dependent claims.

Claims 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's claim 36 is directed to a reagent kit for an enzyme activity assay comprising the ready-to-use enzyme substrate composition comprising paranitrophenyl phosphate, a buffer, charcoal, and

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an enzyme. Claim 37 requires the enzyme to be alkaline phosphatase or acid phosphatase. It is not clear from the language if the enzyme, either alkaline phosphatase or acid phosphatase, is included in the substrate composition, or if it is included in the kit, packaged separately.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Siegenthaler (*Mitteilungen aus dem Lebensmitteluntersuchung und Hygiene*, 1959).

Siegenthaler teaches a method of purifying a solution of sodium paranitrophenyl phosphate by filtering it through activated charcoal. The sodium paranitrophenyl phosphate is in a buffered solution, therefore it is solubilized, and filtering through activated charcoal requires the charcoal to contact the paranitrophenyl phosphate (See Pg 2-3) (Claims 1, 2, and 8). The then stabilized paranitrophenyl phosphate is collected, substantially free of the charcoal (See Pg 3) (Claim 9). Siegenthaler teach the same process of contacting paranitrophenyl phosphate with activated charcoal as in the current application, and thus the stabilized paranitrophenyl phosphate formed by Siegenthaler is one and the same as the stabilized paranitrophenyl phosphate formed in the current application. Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 4-7, 22-25, 30-31, 32-37 & 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegenthaler (*Mitteilungen Aus Der Gebiete Der Lebensmitteluntersuchung Und Hygiene*, 1956), in view of Modrovich (US Patent 4,132,598), and in light of HowStuffWorks.com and Sigma (Product Catalog, 2004).

Siegenthaler teaches a method of purifying a solution of sodium paranitrophenyl phosphate by filtering it through activated charcoal. The sodium paranitrophenyl phosphate is in a buffered solution, therefore it is solubilized, and filtering through activated charcoal requires the charcoal to contact the paranitrophenyl phosphate. The then stabilized paranitrophenyl phosphate is collected and is substantially free of the charcoal (See Pg 2-3). Siegenthaler teach the same process of contacting paranitrophenyl phosphate with activated charcoal as in the current application, and thus the stabilized paranitrophenyl phosphate formed by Siegenthaler is one and the same as the stabilized paranitrophenyl phosphate formed in the current application.

It is clearly an unexplained property of the activated charcoal to substantially stabilize paranitrophenyl phosphate so that it retains its ability to be used as an indicator in the phosphatase test. Therefore, though Siegenthaler teaches filtering the paranitrophenyl phosphate through a layer of activated charcoal, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add activated charcoal to a solution of solubilized paranitrophenyl phosphate, thereby creating a composition of stabilized, solubilized phenyl phosphate comprising a buffer, paranitrophenyl phosphate, and a stabilizing amount of charcoal (which applicant also calls a ready-to-use enzyme substrate) (Claims 22, 23, 24, 30 & 31). One would have been motivated to add the activated charcoal to the solution of solubilized paranitrophenyl phosphate in buffer in order to allow more reaction time with the charcoal, thereby ensuring complete stabilization of the paranitrophenyl phosphate. One would have expected success because Siegenthaler demonstrates the unexplained property of activated charcoal to stabilize paranitrophenyl phosphate, and teaches that the substrate can be re-filtered, and the charcoal can

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be reused; therefore there is no evidence that prolonged exposure to the activated charcoal would have any adverse effects (See Pg 2-3).

Siegenthaler teaches adding about 0.25g of paranitrophenyl phosphate in about 50 cm³ of buffer, which is approximately 50 mL; therefore Siegenthaler stabilizes approximately 5 g/L of paranitrophenyl phosphate by contacting the PNPP with a stabilizing amount of activated charcoal and creates a stabilized, solubilized phenyl phosphate comprising a buffer, paranitrophenyl phosphate, and a stabilizing amount of charcoal (which applicant also calls a ready-to-use enzyme substrate) (See Pg. 2-3 and teachings above). Though 5 g/L is slightly more than claimed by applicant, it would be obvious to use a lower concentration of PNPP and obtain the same results, as, for example, 1.5 g/L of PNPP would certainly be stabilized by the same amount of activated charcoal that stabilizes 5 g/L (Claims 4, 5, 25, 34 & 35). Siegenthaler does not disclose the concentration of the charcoal used, instead he describes about 2 cm of activated charcoal being packed into a filter tube (See Pg. 2-3). Siegenthaler does disclose that the charcoal can be reused, until the filtration effect is no longer effective, therefore it is clear that an excess of charcoal can be used to contact the solution, as the unsaturated charcoal can be reused. Therefore as long as a sufficient amount of charcoal is used, and the stabilized solution is separated from the charcoal before use in the phosphatase test, the concentration of charcoal added to the solution would be routinely optimized by one of ordinary skill in the art (Claims 6, 7, 32 & 33). The amount of charcoal necessary would be determined without undue experimentation by simply performing the stabilization with different amounts of charcoal and then observing the solution, a color change to yellow indicates that free p-nitrophenol has been detected, and the solution must be re-contacted with a greater amount of charcoal (See Pg. 2). Therefore, it is clear that the various proportions and concentrations of the PNPP and charcoal used in the claimed composition are result effective variables, and would be routinely optimized by one of ordinary skill in the art in practicing the invention to ensure a sufficient amount of charcoal is provided for the working concentration of PNPP.

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Siegenthaler teaches the composition of stabilized, solubilized paranitrophenyl phosphate comprising paranitrophenyl phosphate, buffer, and activated charcoal to act as a substrate for a phosphatase test (See Pg 1-3); therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to also include the phosphatase enzyme and market the composition and the enzyme as a reagent kit. One of ordinary skill in the art would have been motivated to include the phosphatase enzyme so that the phosphatase test can be performed, which was Siegenthaler's original intention for stabilizing the PNPP (Claim 36). Though Siegenthaler does not specifically describe the phosphatase enzyme as either alkaline phosphatase or acid phosphatase, he does teach the enzymatic reaction to occur in a pH range of about 10.0, therefore he is referencing the alkaline phosphatase (See Pg 1) (Claim 37). However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively use an acid phosphatase, if the buffer used was acidic. One would have been motivated to use, and expected success with an acid phosphatase if the buffer used to solubilize the paranitrophenyl phosphate was acidic because the phosphatase enzymes are pH specific.

Finally, because it has been deemed obvious to add activated charcoal to the solution of solubilized paranitrophenyl phosphate to create a composition of stabilized paranitrophenyl phosphate comprising solubilized paranitrophenyl phosphate, buffer, and activated charcoal (see teachings above), it would also be obvious to add the activated charcoal to the brown bottle, which Siegenthaler uses to store the paranitrophenyl phosphate, and then add the solution of solubilized paranitrophenyl phosphate in buffer to the bottle for stabilization and storage (See Pg 3). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a bottle (which applicant calls a vessel) with activated charcoal, wherein the charcoal is on the surface of the vessel so that it would contact the solution of paranitrophenyl phosphate when it was added to the bottle (vessel) (Claims 41 & 42). One would have been motivated to create a vessel with activated charcoal on the inside surface so that the solubilized solution of paranitrophenyl phosphate could easily be poured into the vessel. One

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would have been motivated to add the solution of solubilized paranitrophenyl phosphate to the activated charcoal for the reasons described above, specifically to allow more reaction time with the charcoal, thereby ensuring complete stabilization of the paranitrophenyl phosphate. One would have expected success using a bottle with activated charcoal because Siegenthaler teaches storing the paranitrophenyl phosphate in a bottle, and one would expect the charcoal to successfully stabilize the paranitrophenyl phosphate because Siegenthaler demonstrates the unexplained property of activated charcoal to stabilize paranitrophenyl phosphate, and teaches that the substrate can be re-filtered, and the charcoal can be reused, therefore there is no evidence that prolonged exposure to the activated charcoal would have any adverse effects (See Pg 2-3).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 3, 26-29, 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegenthaler (*Mitteilungen Aus Der Gebiete Der Lebensmitteluntersuchung Und Hygiene*, 1956), in view of Modrovich (US Patent 4,132,598), and in light of HowStuffWorks.com and Sigma (Product Catalog, 2004).

Siegenthaler teaches a method of purifying a solution of sodium paranitrophenyl phosphate by filtering it through activated charcoal. The sodium paranitrophenyl phosphate is in a buffered solution, therefore it is solubilized, and filtering through activated charcoal requires the charcoal to contact the paranitrophenyl phosphate. The then stabilized paranitrophenyl phosphate is collected and is substantially free of the charcoal, this stabilized solution of paranitrophenyl phosphate can then be stored in brown bottles in a cool environment (See Pg 3). Siegenthaler teach the same process of contacting paranitrophenyl phosphate with activated charcoal as in the current application, and thus the stabilized

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paranitrophenyl phosphate formed by Siegenthaler is one and the same as the stabilized paranitrophenyl phosphate formed in the current application.

Therefore, though Siegenthaler teaches filtering the paranitrophenyl phosphate through a layer of activated charcoal, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add activated charcoal to a solution of solubilized paranitrophenyl phosphate, thereby creating a composition of stabilized, solubilized phenyl phosphate comprising a buffer, paranitrophenyl phosphate, and a stabilizing amount of charcoal (which applicant also calls a ready-to-use enzyme substrate). One would have been motivated to add the activated charcoal to the solution of solubilized paranitrophenyl phosphate in buffer in order to allow more reaction time with the charcoal, thereby ensuring complete stabilization of the paranitrophenyl phosphate. Additionally, because paranitrophenyl phosphates are known to hydrolyze in aqueous solutions (Modrovich col. 4, ln 50-58), one would have been motivated to include the activated charcoal to protect and stabilize the substrate for storage purposes. One would have expected success because Siegenthaler demonstrates the unexplained property of activated charcoal to stabilize paranitrophenyl phosphate, and teaches that the substrate can be re-filtered, and the charcoal can be reused, therefore there is no evidence that prolonged exposure to the activated charcoal would have any adverse effects.

Siegenthaler does not provide specific details, such as the pH of the buffer, the amounts of paranitrophenyl phosphate used, or the amount of activated charcoal used. However, Modrovich teaches a similar method of stabilizing labile organic substrates, such as paranitrophenyl phosphate, though he uses phenol as a stabilizing agent instead of activated charcoal, he does disclose the details required for the substrate to be used in the phosphatase test (See col. 3, ln 59- col.5, ln 28).

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Modrovich teaches an appropriate buffer for solubilizing the PNPP for an alkaline phosphatase test should have a pH of about 10-10.5, however it can range from 9.5-10.7 (See col. 7, ln 15-18). Modrovich uses AMP, and teaches other suitable buffers include AMP, TEA, TRIS buffers, and DEA (See col. 6, ln 9-12 & col. 7, ln 9-12). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use any alkaline buffers, including BIS-TRIS (pH 9.0-11.0) and AMPD (pH 7.8-9.7), which produce alkaline pH (Sigma Product Catalog) to solubilized the paranitrophenyl phosphate for the method of stabilizing the PNPP, and for the composition of stabilized PNPP, as disclosed by Siegenthaler (Claims 3, 27 & 28). The skilled artisan would have been motivated to use different buffers based on what was available in the lab at the that time, and would have expected success with any buffer which would produce an alkaline pH of about 9.5-10.7, as suggested by Modrovich, because buffers do not interact with the substrates, they only alter the pH.

Modrovich also adds magnesium salts to his PNPP composition. Modrovich teaches the presence of magnesium ions, from magnesium salt, is recommended in the phosphatase test to activate the phosphatase enzyme (See col. 7, ln 1-3). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to add magnesium to the solution of solubilized paranitrophenyl phosphate, buffer, and activated charcoal of Siegenthaler (Claim 29). The skilled artisan would have been motivated to add magnesium to the composition, and have expected success, because Modrovich teach that magnesium activates the phosphatase enzyme during the phosphatase test, and Siegenthaler does teach that the composition of stabilized paranitrophenyl phosphate is to be used for phosphatase testing (See Modrovich col. 7, ln 1-3; Siegenthaler Pg 1-2). By adding magnesium to the solubilized paranitrophenyl phosphate, Siegenthaler's method becomes (a) solubilizing paranitrophenyl phosphate in an aqueous buffered solvent to provide a paranitrophenyl phosphate solution, (b) adding magnesium, in the form of a magnesium salt, to the paranitrophenyl phosphate solution, (c) filtering the solution through activated charcoal (which applicant calls contacting the solution with a stabilizing

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amount of charcoal), and (d) storing the solution in bottles (which applicant calls sealing the solution) (See Pg 2-3). Though Siegenthaler does not specifically state the bottles in which the solution is stored are sealed, it appears obvious that the bottles were supplied with a cap, which would have sealed the solutions (Claims 38 & 39). Furthermore, because the solution of solubilized paranitrophenyl phosphate and magnesium compound in buffer was filtered through activated charcoal and collected, it was substantially free of charcoal at the time of sealing (Claim 40).

Finally, Modrovich teach a sodium salt of PNPP can also be used for the phosphatase test, and can be stabilized in his method (See col. 7, ln 66- col. 8, ln 6). It would have further been obvious to one of ordinary skill in the art at the time the invention was made to use a solubilized ammonia or magnesium salt of paranitrophenyl phosphate to create the solubilized solution of paranitrophenyl phosphate, as taught by Siegenthaler (Claim 26). The skilled artisan would have been motivated to use an ammonia or magnesium salt of paranitrophenyl phosphate and expected success because Modrovich teach a sodium salt of PNPP can be used and, once in solution, the paranitrophenyl phosphate disassociates from the ammonia, magnesium, or sodium ion, and is the same.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

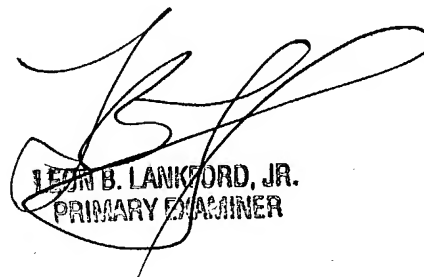
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M Ford whose telephone number is 571-272-2936. The examiner can normally be reached on M-F 7:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Allison M Ford
Examiner
Art Unit 1651



LEON B. LANKFORD, JR.
PRIMARY EXAMINER